ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

Medicinal product no longer authorised

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Staquis 20 mg/g ointment

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One g of ointment contains 20 mg of crisaborole.

Excipients with known effect

Propylene glycol, 90 mg/g of ointment

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Ointment.

White to off-white ointment.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Staquis is indicated for treatment of mild to moderate atopic dermatitis in adults and paediatric patients from 2 years of age with ≤ 40% body surface area (BSA) affected.

4.2 Posology and method of administration

Posology

Adults

A layer of ointment is to be applied twice daily to affected areas.

The ointment should only be applied to affected skin areas up to a maximum of 40% BSA.

The ointment can be used on all skin areas except on the scalp. Use on the scalp has not been studied.

The ointment can be used twice daily for up to 4 weeks per treatment course. If any signs and/or symptoms persist, or new areas affected with atopic dermatitis appear, further treatment course(s) can be used as long as the application does not exceed 40% BSA (see section 5.1).

Use of the ointment should be discontinued if signs and/or symptoms on treated areas persist after 3 consecutive treatment courses of 4 weeks each or if the signs and/or symptoms worsen during treatment.

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Paediatric population

For children and adolescents (2-17 years) the posology is the same as for adults.

The safety and efficacy of Staquis in children less than 2 years of age has not been established. No data are available.

Special populations

Hepatic impairment
Clinical studies in subjects with hepatic impairment have not been conducted. However, dosage adjustment is not expected to be necessary in subjects with mild to moderate hepatic impairment.

Renal impairment
Clinical studies in subjects with renal impairment have not been conducted. However, dosage adjustment is not expected to be necessary in this patient population.

Elderly
Atopic dermatitis is uncommonly observed in patients aged 65 years and over. Clinical studies of Staquis did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger subjects (see section 5.1). However, dosage adjustment is not expected to be necessary in this patient population.

Method of administration

The ointment is for cutaneous use only.

The ointment is not for ophthalmic, oral, or intravaginal use (see section 4.4).

Staquis has not been specifically studied under occlusion. However, clinical experience available for use of the ointment under occlusion (i.e., nappies or clothing) has not shown the necessity for any dosage adjustment.

Patients should be instructed to wash their hands after applying the ointment, unless it is their hands that are being treated. If someone else applies the ointment to the patient, they too should wash their hands after application.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

The ointment is not for ophthalmic, oral, or intravaginal use (see section 4.2). In cases of accidental exposure in the eyes or mucous membranes, the ointment should be thoroughly wiped off and/or rinsed with water.

Available data indicate that local skin reactions, such as burning or stinging, may be more likely to occur on sensitive skin areas (such as the face and neck).

Hypersensitivity

Hypersensitivity, including contact urticaria, has occurred in patients treated with Staquis. Hypersensitivity should be suspected in the event of severe pruritus, swelling and erythema at the application site or at a distant site. If signs and symptoms of hypersensitivity occur, Staquis should be discontinued immediately and appropriate therapy should be initiated.

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Excipients with known effect

This medicine contains 90 mg propylene glycol in each gram of ointment.

4.5 Interaction with other medicinal products and other forms of interaction

Neither crisaborole nor its two main metabolites are expected to cause drug interactions by induction or inhibition of cytochrome P450 (CYP) enzymes based on *in vitro* and *in vivo* data (see section 5.2).

Based on *in vitro* data, concomitant administration of Staquis and CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, erythromycin, clarithromycin, ritonavir) or CYP1A2 inhibitors (e.g., ciprofloxacin, fluvoxamine) can increase systemic crisaborole concentrations (see section 5.2).

Staquis has not been evaluated in combination with other cutaneous medicinal products used to treat mild to moderate atopic dermatitis and co-application on the same skin areas is not recommended. Emollients may be used on other areas of skin not affected by atopic dermatitis; co-application of emollients with Staquis on the same skin areas is not recommended.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of crisaborole in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Staquis during pregnancy.

Breast-feeding

Animal studies on milk excretion after topical application were not conducted. Staquis is systemically absorbed. It is unknown whether crisaborole or its metabolites or excipients are excreted in human milk following topical application of the ointment or has an effect on human milk production. The lack of clinical data during breast-feeding precludes a clear determination of the risk of Staquis to a breastfed infant. Therefore, because of the potential for adverse reactions in breastfed infants, Staquis should not be used in breast-feeding women.

Fertility

Reproduction studies in male or female rats using oral administration of crisaborole revealed no effects on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Staquis has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions are application site reactions (6.0%), including application site pain, e.g., burning or stinging (4.4%). Generally, application site pain was noted early in the treatment period and was transient in nature, resolving spontaneously.

Tabulated list of adverse reactions

Adverse reactions are ranked under headings of frequency, with the most frequent first, using the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to

Medicinal product no longer authorised

< 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data).

Table 1: Adverse reactions

Immune system disorders	
Uncommon	Hypersensitivity
Skin and subcutaneous tissue disorders	
Uncommon	Urticaria contact
General disorders and administration site conditions	
Common	Application site reactions (e.g., application site pain[1], application site pruritus, application site dermatitis, application site erythema, application site irritation, application site urticaria)

[1] Refers to skin sensations such as burning or stinging.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Overdose following cutaneous administration is unlikely. If too much of the ointment has been applied, the excess can be wiped off.

In cases of accidental ophthalmic, oral mucosa, or intravaginal exposure, the ointment should be thoroughly wiped off and/or rinsed with water (see sections 4.2 and 4.4).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other dermatological preparations, agents for dermatitis, excluding corticosteroids, ATC code: D11AH06

Mechanism of action

Crisaborole is an anti-inflammatory benzoxaborole phosphodiesterase-4 (PDE4) inhibitor that suppresses secretion of certain cytokines, such as tumour necrosis factor-α (TNF-α), interleukins (IL-2, IL-4, IL-5), and interferon gamma (IFNγ), and improves skin barrier function as measured by transepidermal water loss (TEWL). Crisaborole applied on atopic dermatitis lesions of patients reduces expression of atopic inflammation associated chemokines including CCL17, CCL18, and CCL22.

Clinical efficacy and safety

Two multicentre, randomised, double-blind, parallel-group, vehicle-controlled trials (Trials 1 and 2), identical in design, included a total of 1,522 subjects 2 to 79 years of age. 61.9% of subjects were 2-11 years old, 24.4% of subjects were 12-17 years old, 13.3% of subjects were 18-64 years old, and 0.5% of subjects were 65 years of age or older; the number of subjects ≥ 18 years of age was limited. The treatable BSA ranged from 5% to 95% (mean = 18.3%, standard deviation [SD] = 17.8%; 9.6% of subjects had > 40% treatable BSA); the trials did not include sufficient numbers of subjects with > 40% treatable BSA to determine the safety and efficacy of Staquis in this subpopulation. At baseline (pooled study data), 38.5% of the subjects had an Investigator's Static Global Assessment (ISGA)

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score of 2 (Mild), and 61.5% had an ISGA score of 3 (Moderate), in the overall assessment of atopic dermatitis (erythema, induration/papulation, and oozing/crusting) on a severity scale of 0 to 4.

In both trials, subjects were randomised 2:1 to receive Staquis or vehicle applied twice daily for 28 days. The primary efficacy endpoint was the proportion of subjects at Day 29 who achieved an ISGA grade of Clear (score of 0) or Almost Clear (score of 1) with at least a 2-grade improvement from baseline, comparing Staquis-treated subjects to vehicle-treated subjects. In both trials, a statistically significantly greater percentage of subjects achieved this endpoint in the Staquis-treated group compared with the vehicle-treated group.

The secondary efficacy endpoints were the proportion of subjects at Day 29 with an ISGA grade of Clear or Almost Clear and the time to achieve an ISGA grade of Clear or Almost Clear with at least a 2-grade improvement from baseline.

The safety and efficacy of Staquis on sensitive skin areas (such as the face and neck) compared to nonsensitive skin areas (such as the arms and legs) were not separately assessed in the clinical trials.

Efficacy results from the two trials are summarised in Tables 2 and 3. The Kaplan-Meier plots for the time to achieve an ISGA score of Clear or Almost Clear with at least a 2-grade improvement from baseline are provided in Figures 1 and 2. The log-rank test p-values for both trials were < 0.001.

Table 2: Efficacy outcomes in subjects with mild to moderate atopic dermatitis

	Trial 1		**Trial 2**	
	Staquis (N = 503)	**Vehicle (N = 256)**	**Staquis (N = 513)**	**Vehicle (N = 250)**
ISGA score of Clear or Almost Clear with at least a 2-grade improvement from baseline at Day 29	32.8%	25.4%	31.4%	18.0%
95% CI[a]	(28.6, 37.0)	(19.9, 30.9)	(27.3, 35.5)	(13.2, 22.9)
p-value	0.038[b]		< 0.001[b]	
ISGA of Clear or Almost Clear at Day 29	51.7%	40.6%	48.5%	29.7%
95% CI[a]	(47.2, 56.1)	(34.4, 46.8)	(44.1, 52.9)	(23.9, 35.5)
p-value	0.005[b]		< 0.001[b]	

[a] Confidence Interval (CI) from normal approximation.
[b] p-value from a logistic regression (with Firth option) test with factors of treatment group and analysis centre after adjusted for multiple imputation.

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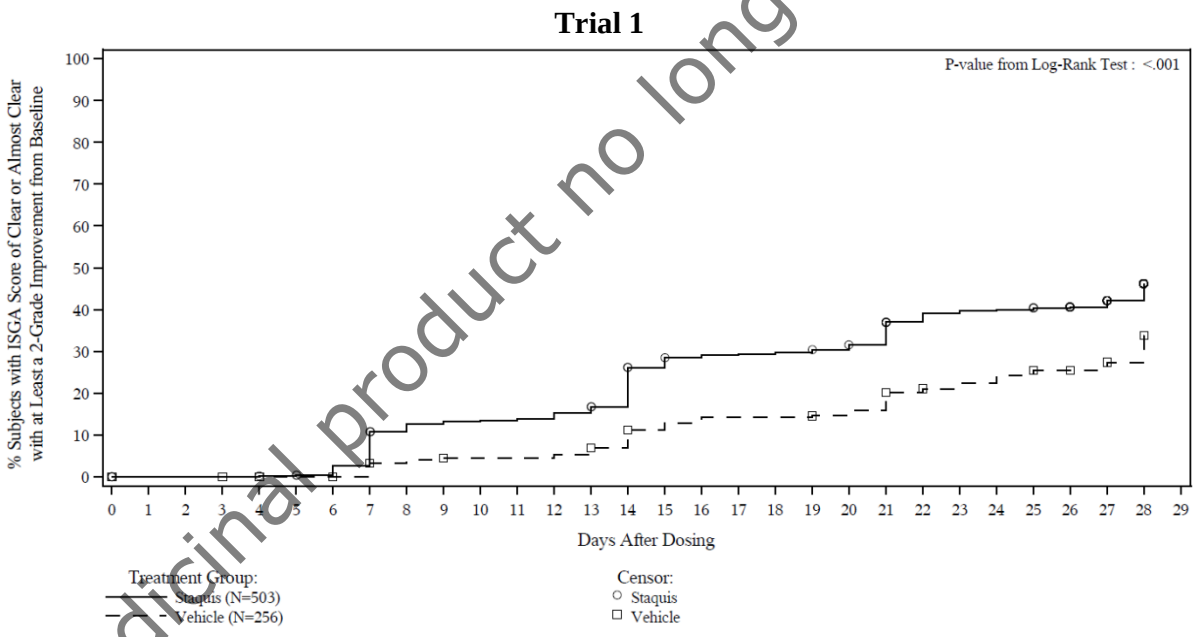
Table 3: Post-hoc efficacy outcomes in subjects with mild to moderate atopic dermatitis with ≤ 40% BSA affected

	Trial 1		Trial 2	
	Staquis (N = 446)	**Vehicle (N = 231)**	**Staquis (N = 465)**	**Vehicle (N = 234)**
ISGA score of Clear or Almost Clear with at least a 2-grade improvement from baseline at Day 29	34.1%	25.5%	32.6%	18.8%
95% CI[a]	(29.7, 38.6)	(19.7, 31.3)	(28.3, 36.9)	(13.7, 24.0)
p-value	0.022[b]		<0.0001[b]	
ISGA of Clear or Almost Clear at Day 29	53.8%	41.9%	51.0%	30.9%
95% CI[a]	(49.1, 58.5)	(35.3, 48.4)	(46.4, 55.6)	(24.8, 37.0)
p-value	0.0041[b]		<0.0001[b]	

[a] Confidence Interval (CI) from normal approximation.
[b] p-value from a logistic regression (with Firth option) test with factors of treatment group and analysis centre after adjusted for multiple imputation.

Figure 1: Kaplan-Meier plot of Time to ISGA score of Clear or Almost Clear with at least a 2-grade improvement from baseline for subjects with mild to moderate atopic dermatitis



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Trial 2

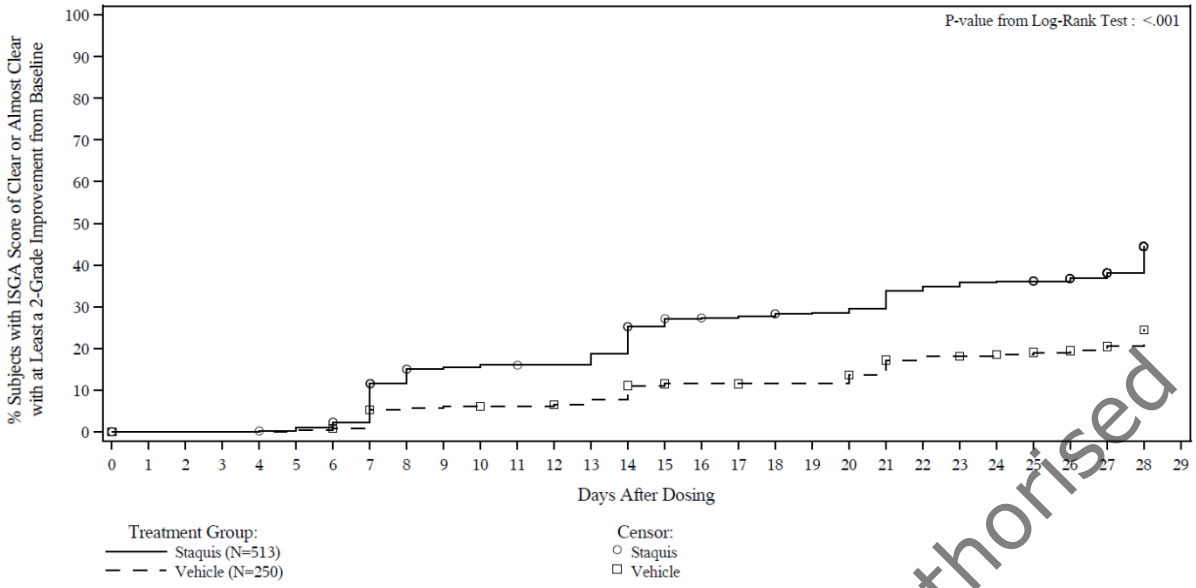
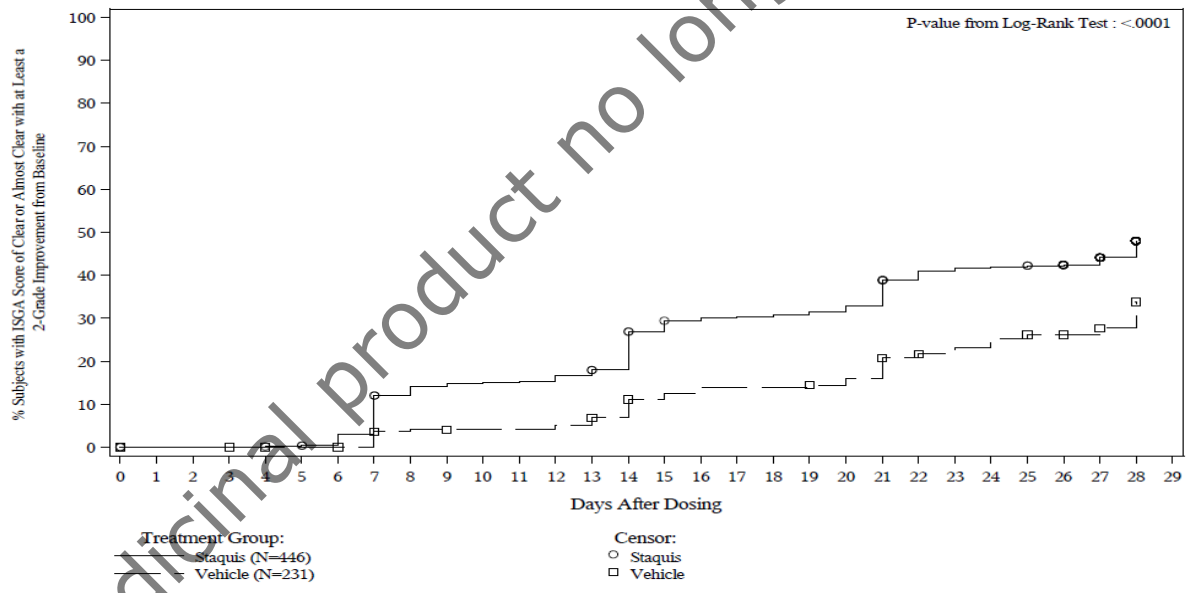


Figure 2: Post-hoc Kaplan-Meier plot of Time to ISGA score of Clear or Almost Clear with at least a 2-grade improvement from baseline for subjects with mild to moderate atopic dermatitis with ≤ 40% BSA affected

Trial 1



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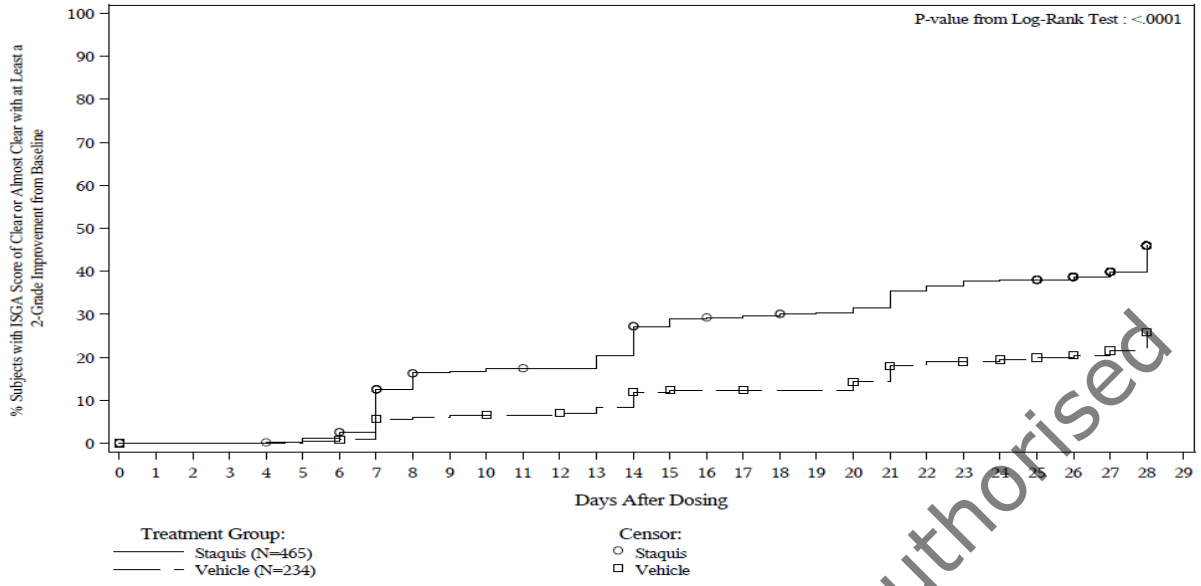
Trial 2



The pooled primary efficacy results by race category are summarised in Table 4.

Table 4: Summary of subjects achieving ISGA score of Clear or Almost Clear with at least a 2-grade improvement from baseline at Day 29 by race category – Trial 1 and 2 pooled

	Staquis (N = 1016)		Vehicle (N = 506)	
Race Category	**n**	**Rate**	**n**	**Rate**
American Indian or Alaska Native	11	18.0%	5	0.0%
Asian	52	17.7%	27	13.4%
Black or African American	285	32.1%	139	24.6%
Native Hawaiian or Other Pacific Islander	7	42.9%	8	17.0%
White	617	33.5%	306	22.3%
Other	44	31.9%	21	16.3%

N = Number of subjects in each treatment group
n = Number of subjects in each sub-group category by treatment group

One multicentre, single-arm, open-label long-term safety trial (Trial 3) included a total of 517 subjects 2 to 72 years of age (59.6% of subjects were 2-11 years old, 28.2% of subjects were 12-17 years old, 11.8% of subjects were 18-64 years old, and 0.4% of subjects were 65 years of age or older) with a 5% to 95% treatable BSA. Subjects at participating investigator sites (a subset of sites that participated in Trials 1 and 2) who completed Trials 1 or 2 without safety events that precluded further treatment with Staquis were eligible.

Subjects participated in the study in 28-day treatment courses for up to 48 weeks. Subjects received Staquis for a variable number of treatment courses intermittently based on disease severity as determined by the ISGA at the beginning of each 28-day treatment course: subjects received open-label treatment with Staquis twice daily (on-treatment when ISGA was Mild or worse [≥ 2]) or no treatment (off-treatment when the ISGA was Clear [0] or Almost Clear [1]). Discontinuation from

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the study was to occur if there was no improvement in the subject's ISGA after 3 consecutive treatment courses of treatment with Staquis.

Trial 3 did not include an efficacy endpoint; Staquis efficacy response based on ISGA determined the extent of intermittent use of Staquis for up to 48 weeks. Overall, subjects received a mean of 6.2 on-treatment courses (out of a possible 13 on-treatment courses including the 28-day treatment period in Trials 1 or 2). The mean number of consecutive on-treatment courses was 3.6 and the mean number of consecutive off-treatment courses was 2.5.

QT study results

Results from a thorough QT study of Staquis applied to 60% BSA in healthy volunteers did not demonstrate QT prolongation. Although healthy volunteers had lower crisaborole concentrations compared to patients with atopic dermatitis, clinical studies of Staquis did not identify any cardiac effects including prolongation of QT interval.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Staquis in one or more subsets of the paediatric population for the treatment of atopic dermatitis (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

The pharmacokinetics (PK) of Staquis were investigated in 33 paediatric subjects 2 to 17 years of age with mild to moderate atopic dermatitis and a mean ± SD BSA involvement of 49 ± 20% (range 27% to 92%). In this study, subjects applied approximately 3 mg/cm^2 of Staquis ointment (dose range was approximately 6 g to 30 g per application) twice daily for 8 days. Plasma concentrations were quantifiable in all subjects. The mean ± SD maximum plasma concentration (C_{max}) and area under the concentration time curve from 0 to 12 hours post dose (AUC_{0-12}) for crisaborole on Day 8 were 127 ± 196 ng/mL and 949 ± 1240 ng*h/mL, respectively. Systemic concentrations of crisaborole were at steady state by Day 8. Based on the ratios of AUC_{0-12} between Day 8 and Day 1, the mean accumulation factor for crisaborole was 1.9. Systemic exposure (C_{max} and AUC_{0-12}) of crisaborole and its main metabolites increased with increasing % BSA treated.

The studies were performed with a different formulation of crisaborole which, unlike Staquis, contained butylhydroxytoluene (BHT). *In vitro* permeation testing (IVPT) was performed in intact skin to support therapeutic equivalence between the BHT-containing and the no-added BHT formulations. Although the results were inconclusive and highly variable, a possible slight increase in permeation is not expected to influence the benefit-risk profile of the product in patients with up to 40% BSA affected to a clinically relevant extent.

Distribution

Based on an *in vitro* study, crisaborole is 97% bound to human plasma proteins.

Biotransformation and elimination

Crisaborole is substantially metabolised into inactive metabolites. The main metabolite 5-(4-cyanophenoxy)-2-hydroxyl benzylalcohol (metabolite 1), is formed via multiple CYP enzymes including CYP3A4, 1A2 and hydrolysis; this metabolite is further metabolised into downstream metabolites, among which 5-(4-cyanophenoxy)-2-hydroxyl benzoic acid (metabolite 2), formed via oxidation, is also a main metabolite. PK of metabolites 1 and 2 were assessed in the PK study described above and the systemic concentrations were at or near steady state by Day 8. Based on the ratios of AUC_{0-12} between Day 8 and Day 1, the mean accumulation factors for metabolites 1 and 2

Medicinal product no longer authorised

were 1.7 and 6.3, respectively. The mean ± SD C_{max} and AUC_{0-12} for metabolite 2 on Day 8 were 1850 ± 1830 ng/mL and 18200 ± 18100 ng*h/mL, respectively. Renal excretion of metabolites is the major route of elimination. Approximately 25% of the radiolabelled dose was absorbed and predominantly excreted in the urine.

Drug interactions

Potential for crisaborole to influence the PK of other medicinal products
In vitro studies using human liver microsomes indicated that under the conditions of clinical use, crisaborole and metabolite 1 are not expected to inhibit CYP1A2, 2B6, 2C8, 2C9, 2C19, and 3A4.

In vitro human liver microsomes studies for metabolite 2 showed that it did not inhibit activities of CYP2C19, 2D6, and 3A4; was a weak inhibitor of CYP1A2 and 2B6; and a moderate inhibitor of CYP2C8 and 2C9. The most sensitive enzyme, CYP2C9, was further investigated in a clinical trial using warfarin as a CYP2C9 substrate. The results of this study showed no drug interaction potential.

In vitro studies indicate that under the condition of clinical use, crisaborole and metabolites 1 and 2 are not expected to induce CYP enzymes.

Based on *in vitro* data, crisaborole is metabolised to some extent (<30%) via CYP3A4 and CYP1A2. Concomitant administration of Staquis and potent CYP3A4 or CYP1A2 inhibitors may result in increases in crisaborole systemic exposure.

In vitro studies showed that crisaborole and metabolite 1 did not inhibit the activities of uridine diphosphate (UDP)-glucuronosyltransferase (UGT) 1A1, 1A4, 1A6, 1A9, 2B7, and 2B15. Metabolite 2 did not inhibit UGT1A4, 1A6, 2B7, and 2B15. Metabolite 2 showed weak inhibition of UGT1A1; however, no clinically significant drug interactions are expected between crisaborole (and its metabolites) and UGT1A1 substrates at therapeutic concentrations. Metabolite 2 showed moderate inhibition of UGT1A9 and may result in a moderate increase of the concentrations of sensitive UGT1A9 substrates, such as propofol. A clinically relevant interaction between metabolite 2 and propofol is not anticipated due to the posology and method of administration of propofol (intravenous infusion or injection with titration to clinical effect for anaesthesia or sedation). Drug interaction studies with sensitive UGT1A9 substrates have not been conducted.

In vitro studies indicate that under the condition of clinical use, crisaborole and metabolites 1 and 2 are not expected to cause clinically significant interactions with substrates of transporters such as P-glycoprotein, breast cancer resistance protein (BCRP) and organic anionic or cationic transporters.

5.3 Preclinical safety data

Preclinical data from studies conducted *in vitro* or *in vivo* by the oral and dermal routes of administration reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated-dose toxicity, genotoxicity, juvenile toxicity, or toxicity to reproduction and development.

A drug-related increased incidence of benign granular cell tumours in the uterus with cervix and vagina (combined) was noted in crisaborole-treated female rats at oral doses approximately 2 times the mean human systemic exposure in maximum use conditions. The clinical relevance of this finding is unknown, however given the tumour type and benign status in a single species and single sex, the relevance to humans is considered to be low.

Medicinal product no longer authorised

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Paraffin, white soft
Propylene glycol (E 1520)
Glycerol monostearate 40-55 (Type I)
Paraffin, hard
Sodium calcium edetate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

After first opening the container: 1 year.

6.4 Special precautions for storage

Do not store above 25 ºC. Do not freeze.

Keep the tube tightly closed.

6.5 Nature and contents of container

Multi-layered laminate tube with a high density polyethylene tube head with a peel seal, and a white polypropylene cap closure. The exterior layer of the tube consists of seven layers (low-density polyethylene, white high-density polyethylene, high-density polyethylene, low-density polyethylene, ethylene-acrylic acid, foil, and ethylene-acrylic acid). The inner lining consists of linear low-density polyethylene.

Tubes of 2.5 g, 30 g, 60 g, and 100 g. Six tubes per carton for the 2.5 g tubes. One tube per carton for the 30 g, 60 g, and 100 g tubes.

Not all tube sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

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8. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1421/001
EU/1/19/1421/002
EU/1/19/1421/003
EU/1/19/1421/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 March 2020

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

Medicinal product no longer authorised

Medicinal product no longer authorised

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Pfizer Service Company BVBA
Hoge Wei 10
1930 Zaventem
Belgium

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

Medicinal product no longer authorised

ANNEX III

LABELLING AND PACKAGE LEAFLET

Medicinal product no longer authorised

A. LABELLING

Medicinal product no longer authorised

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (2.5 g, 30 g, 60 g, 100 g)

1. NAME OF THE MEDICINAL PRODUCT

Staquis 20 mg/g ointment
crisaborole

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 g of ointment contains 20 mg of crisaborole.

3. LIST OF EXCIPIENTS

Paraffin, white soft; propylene glycol (E 1520); glycerol monostearate 40-55 (Type I); paraffin, hard; sodium calcium edetate.

Read the package leaflet before use.

4. PHARMACEUTICAL FORM AND CONTENTS

Ointment

6 tubes (2.5 g)
1 tube (30 g)
1 tube (60 g)
1 tube (100 g)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Cutaneous use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Medicinal product no longer authorised

9. SPECIAL STORAGE CONDITIONS

Do not store above 25 ºC. Do not freeze.

Keep the tube tightly closed.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Pfizer Europe MA EEIG
Boulevard de la Plaine 17
1050 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1421/001	6 tubes (2.5 g)
EU/1/19/1421/002	1 tube (30 g)
EU/1/19/1421/003	1 tube (60 g)
EU/1/19/1421/004	1 tube (100 g)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Staquis

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC

Medicinal product no longer authorised

SN
NN

Medicinal product no longer authorised

PARTICULARS TO APPEAR ON THE INNER PACKAGING

TUBE (30 g, 60 g, 100 g)

1. NAME OF THE MEDICINAL PRODUCT

Staquis 20 mg/g ointment
crisaborole

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 g of ointment contains 20 mg of crisaborole.

3. LIST OF EXCIPIENTS

Paraffin (white soft, hard); E 1520; glycerol monostearate; sodium calcium edetate.

Read the package leaflet before use.

4. PHARMACEUTICAL FORM AND CONTENTS

Ointment

30 g
60 g
100 g

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Cutaneous use

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Medicinal product no longer authorised

9. SPECIAL STORAGE CONDITIONS

Do not store above 25 ºC. Do not freeze.

Keep the tube tightly closed.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Pfizer Europe MA EEIG

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1421/002 30 g
EU/1/19/1421/003 60 g
EU/1/19/1421/004 100 g

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

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MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

TUBE (2.5 g)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Staquis 20 mg/g ointment
crisaborole
Cutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

2.5 g

6. OTHER

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B. PACKAGE LEAFLET

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Package leaflet: Information for the patient

Staquis 20 mg/g ointment
crisaborole

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist, or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Staquis is and what it is used for

Staquis contains the active substance crisaborole. Staquis is used on the skin to control the symptoms of mild to moderate atopic dermatitis in adults and children from 2 years of age. Atopic dermatitis, also called atopic eczema, causes skin inflammation, redness, itchiness, dryness, and thickening in people prone to allergies. The ointment should not be used on more than 40% of your body surface area.

Crisaborole, the active substance in Staquis, is thought to work by reducing inflammation and some effects of the immune system (the body's defences).

2. What you need to know before you use Staquis

Do not use Staquis
- if you are allergic to crisaborole or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before using Staquis.

Staquis is not for use in the eyes, mouth, or vagina; therefore, take care not to get this ointment into these areas. If the ointment accidentally gets into these areas, thoroughly wipe off and/or rinse off the ointment with water.

Stop using Staquis immediately and see your doctor if you get an allergic reaction. Symptoms include welts (hives), itching, swelling, and redness that are severe.

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Skin reactions where this medicine is applied, such as burning or stinging, may be more likely to occur on sensitive skin areas such as the face and neck.

Children
Staquis has not been studied in children younger than 2 years of age; therefore, it should not be used in this group of children. Speak to your doctor, pharmacist, or nurse.

Other medicines and Staquis
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Some medicines can affect the levels of Staquis in your body. You should inform your doctor if you are taking medicines containing the following active substances:
- ketoconazole, itraconazole (used to treat fungal infections)
- erythromycin, clarithromycin, ciprofloxacin (used to treat infections)
- ritonavir (used to treat HIV)
- fluvoxamine (used to treat depression).

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine. The effects of this medicine in pregnant women are not known; therefore, do not use Staquis in pregnancy unless you have checked with your doctor that you can use it.

It is not known if Staquis passes into the milk after applying it to the skin. The effects of this medicine in breastfed infants are not known; therefore, Staquis should not be used if you are breast-feeding or are planning to breast-feed.

Driving and using machines
Staquis is unlikely to have an effect on your ability to drive and use machines.

Staquis contains propylene glycol
This medicine contains 90 mg propylene glycol in each gram of ointment.

3. How to use Staquis

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Use in adults
- Apply a layer of the ointment twice daily to affected areas of your skin.
- This medicine can be used on all skin areas except on the scalp.
- The ointment should only be used on up to 40% of your body surface area.
- This medicine is for use on the skin only.
- Wash your hands after applying this medicine, unless it is your hands that are being treated. If someone else applies this medicine to you, they should wash their hands after application.

This medicine can be used twice daily for up to 4 weeks per treatment course. As instructed by your doctor, you can use further treatment course(s) if your atopic dermatitis is not controlled or appears on new areas as long as you do not apply the ointment to more than 40% of your body surface area. If your atopic dermatitis is still there after 12 weeks of therapy, or if your atopic dermatitis gets worse, stop using the medicine and see your doctor.

Moisturisers (emollients) may be used on areas of the skin where Staquis is not applied. Do not use other topical medicines (such as ointments, creams, lotions) on areas of the skin where Staquis is applied without asking your doctor.

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Use in children and adolescents
For children 2 years of age and older, and adolescents the instructions for use are the same as for adults.

If you use more Staquis than you should
If too much Staquis has been applied, the excess should be wiped off.

If you forget to use Staquis
If you forget to apply the ointment at the scheduled time, do it as soon as you remember and then continue your normal dosing schedule.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Allergic reactions may occur uncommonly. Allergic reactions include severe symptoms of:
- hives
- itching
- swelling
- redness.

If you have an allergic reaction, stop using this medicine immediately and talk with your doctor or pharmacist.

Other side effects may include:

Common (may affect up to 1 in 10 people)
- Skin reactions where this medicine is applied such as pain (burning or stinging), itching, rash, redness, irritation, and hives.

The most common skin reaction, pain (burning or stinging), is usually mild to moderate and generally goes away after several applications.

Uncommon (may affect up to 1 in 100 people)
- Allergic reactions: includes severe symptoms of hives, itching, swelling, and redness.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

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5. How to store Staquis

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the tube and carton after “EXP”. The expiry date refers to the last day of that month.

Do not store above 25 ºC. Do not freeze.

Once opened, use the tube within 1 year.

Keep the tube tightly closed.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Staquis contains
- The active substance is crisaborole.
  One g of ointment contains 20 mg of crisaborole.
- The other ingredients are paraffin, white soft; propylene glycol (E 1520 [see section 2]); glycerol monostearate 40-55 (Type I); paraffin, hard; sodium calcium edetate.

What Staquis looks like and contents of the pack
Staquis is a white to off-white ointment. It is supplied in 2.5 g, 30 g, 60 g, and 100 g laminate tubes. There are six tubes per carton for the 2.5 g tubes. There is one tube per carton for the 30 g, 60 g, and 100 g tubes. Not all tube sizes may be marketed.

Each tube comes with a tube head with a peel seal, and a white cap closure.

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Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

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